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Michle C. Barrett — Michael C. Barrett

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Gascoyne *et al.*

Serial No.: 10/743,698

Filed: December 20, 2003

For: METHODS AND APPARATUS FOR ELECTROSMEAR ANALYSIS

Group Art Unit: 1753

Examiner: Jeffrey Thomas Barton

Atty. Dkt. No.: UTXC:760US/MCB

APPEAL BRIEF

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APPEAL BRIEF

MS: APPEAL BRIEF - PATENTS
Commissioner of Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Appellant submits this Appeal Brief to the Board of Patent Appeals and Interferences in response to the final Office Action dated June 28, 2005. The Notice of Appeal was received by the Patent Office on August 31, 2005, as indicated by a stamped postcard. A three-month extension and associated fee is concurrently filed with this Appeal Brief to bring the due date to January 31, 2006. The $250.00 filing fee for this Appeal Brief is also included.

Appellant believes that no additional fees are due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Commissioner is authorized to deduct those fees from Fulbright & Jaworski Deposit Account No. 50-1212/UTXC:760US/MCB. If overpayment is included, the Commissioner is authorized to credit that account.

Please date stamp and return the attached postcard as evidence of receipt.

I. REAL PARTY IN INTEREST

The real party in interest is the assignee, Board of Regents, The University of Texas System.

II. RELATED APPEALS AND INTERFERENCES

No related appeals or interferences are presently pending.

III. STATUS OF THE CLAIMS

Claims 1 through 56 were originally filed on December 22, 2003. In response to the first Office Action mailed on October 27, 2004, claims 1, 12, 16, 44, 49, and 55 were amended. Thus, claims 1-56 are pending on appeal and are the subject of this Brief. A copy of the appealed claims is attached as Appendix A.

IV. STATUS OF AMENDMENTS

No claims were amended subsequent to the Final Office Action.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The invention generally concerns subjecting particles of a sample to a dielectrophoretic force to segregate the particles.[1] *See* Specification, p. 7, second paragraph of the Summary of the Invention. In some embodiments, the subjecting of the particles to a dielectrophoretic force may arise from the application of frequencies exhibiting one or more DEP-FFF and trapping phases. *See* page 18, the paragraph beginning at line 29; *see also* page 19, the paragraph beginning at line 5. Alternatively, in other embodiments, the dielectrophoretic force may arise from current passing through an opening in a dielectric barrier. *See* page 43, the paragraph beginning at line 17.

[1] The claims of the invention are not limited by this summary—the embodiments listed in the summary are exemplary only. Recitation of support in the specification does not imply that is the *only* support that may be found.

In one embodiment, the sample may be subjected to the dielectrophoretic force by simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes. *See* page 8, the paragraph beginning at line 6; *see also* page 32, the paragraph beginning at line 10.

In some embodiments, the first set and/or second set of electrodes may include spiral electrodes. *See* page 26, the paragraph beginning on line 1. In other embodiments, the electrodes may be coupled to the surface. *See* page 20, the paragraph beginning at line 21.

The swept frequency may fall from a maximum intensity to a minimum intensity (*e.g.*, a non-zero intensity) along the length of the surface in a first direction. *See* page 32, the third paragraph of Example 2. The fixed frequency signal may fall from a maximum intensity to a minimum intensity (*e.g.*, a non-zero intensity) along the length of the surface in a second direction, where the second direction may oppose the first direction. *See id.*

In one respect, the intensities of the swept frequency signal and the fixed frequency may vary linearly along the length of the surface. *See* page 32, the third paragraph of Example 2. In other respects, the intensities may vary non-linearly along the length of the surface. *See* page 38, the paragraph beginning at line 11. Alternatively, the intensities may vary by varying a width of electrode buses with distance along the length of the surface. *See id.*

In some embodiments, the swept frequency signal or the fixed frequency signal may be adjusted. *See* page 39, the second paragraph of Example 4. The adjusting may be automated and may be a function of conductivity of a particle suspending medium. *See id.*

The dielectrophoretic force may segregate the particles of the sample into two or more zones of a surface. *See* page 7, second paragraph of the Summary of the Invention. In one embodiment, the particles on the sample may be segregated into two or more zones on a surface,

using, for example, physical barriers. *See* page 7, second paragraph of the Summary of the Invention *see also* page 49, Example 6. In some respects, the segregating of the particles includes a DEP-FFF flow. *See* page 52, Example 8.

In some embodiments, the particles may be segregated into two or more concentric circular zones. *See* page 26, the paragraph beginning at line 11. Alternatively or in addition to the above, the particles may be segregated into two or more zones comprising distinct bands of particles. *See* page 30, Results section of Example 1.

In some respects, the particles may be attached to the surface, thereby defining, for example, a segregated smear (*e.g.,* for uses as a pap smear). *See* page 7, the second and third paragraphs of the Summary of the Invention. In some embodiments, to attach the particles, a dielectrophoretic force may be used. *See id.* In other embodiments, an adhesive coupled to the surface may be used. *See* page 16, the paragraph beginning at line 19. Alternatively, the particles may be allowed to settle on the surface. *See id.*

In other respects, the invention provides filtering the sample by, for example, subjecting the particles to a flow, a cross flow, and a dielectrophoretic force that may oppose the force associated with the cross flow. *See* page 43, first paragraph of the "First Set of Embodiments" of Example 5. The dielectrophoretic force component for filtering the sample may arise from the excitation of electrodes near a dielectric substrate having openings. *See* page 42, the first paragraph under the "Setting Up a Filter" section. In one embodiment, the flow and the cross flow may be substantially perpendicular to one another. *See id.* Alternatively, the flow and the cross flow may not be perpendicular. *See id.*

In other embodiments, the particles of the sample may be fixed. *See* page 22, the paragraph beginning at line 15. Alternatively or in addition to the above, the particles of the sample may be smeared. *See* page 22, the paragraph beginning at line 27.

In some embodiments, growth of particles on a surface may be promoted. *See* page 50, the paragraph beginning at line 4. The particles may include, for example, cells. *See* page 15, the paragraph beginning at line 19.

The invention also provides an apparatus. The apparatus may include a surface and electrodes near the surface. *See* page 15, the paragraph beginning at line 13. In some embodiments, the apparatus may include first and second signal generators. *See* page 32, the paragraph beginning at line 10. The first signal generator may be configured to apply a fixed frequency signal to a first electrode where the fixed frequency signal may fall from a maximum intensity to a minimum intensity along a length of the surface in a first direction. *See id; see also* page 32, the paragraph beginning at line 21. The second signal generator may be configured to apply a swept frequency signal to a second electrode, where the swept frequency signal may fall from a maximum intensity to a minimum intensity along the length of the surface in a second direction opposing the first direction. *See id.* In some embodiments, the fixed frequency and the swept frequency may be applied simultaneously, where the combination generates a dielectrophoretic force configured to segregate particles into two or more zones of the surface. *See* page 8, the paragraph beginning at line 6.

In some embodiments, the apparatus may include a filter. *See* Example 5 beginning on page 40, line 16. The filter may include electrodes near a dielectric substrate having openings. *See* page 42, the paragraph beginning at line 16. The filter may be configured to subject particles

of a sample to a flow, a cross flow, and a dielectrophoretic force that opposes a force associated with the cross flow. *See* page 43, the paragraph beginning at line 5.

In other embodiments, the apparatus may include a physical barrier. *See* page 49, Example 6. The physical barrier may be near the surface and may be configured to attach particles into two or more zones of the surface. *See id; see also* page 7, second paragraph of the Summary of the Invention.

The invention also provides an apparatus for preparing a smear for cytopathology. *See* page 8, the paragraph beginning at line 12. The apparatus may include a dielectrophoretic field flow fractionator that may be configured to subject particles of a sample to a dielectrophoretic force to segregate the particles into two or more zones. *See id.* In one respect, the dielectrophoretic force may include simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes. *See* page 8, the paragraph beginning at line 6; *see also* page 32, the paragraph beginning at line 10.

The apparatus for preparing a smear for cytopathology may also include a dielectrophoretic collector coupled to the dielectrophoretic field flow fractionator. *See* page 8, the paragraph beginning at line 12. In some embodiments, the dielectrophoretic collector and the dielectrophoretic field flow fractionator may be an integral unit. *See* page 23, the paragraph beginning at line 24. The collector may be configured to subject the particles to a dielectrophoretic force to attach the particles to a surface. *See id.*

The apparatus may also include a machine reader coupled to the dielectrophoretic collector and the dielectrophoretic field flow fractionator. *See* page 24, the paragraph beginning at line 18. In some embodiments, the machine reader may be configured to evaluate particles within two or more zones. *See id.*

The apparatus for preparing a smear for cytopathology may also include a fixing stage and a staining stage coupled to the dielectrophoretic collector. *See* page 24, the paragraph beginning at line 4. In some embodiments, the fixing stage, the staining stage, and the dielectrophoretic collector may be an integral unit. *See id.*

The invention also provides a kit in a suitable container for preparing a smear for cytopathology. *See* page 8, the paragraph beginning at line 20. In one embodiment, the kit may also include one or more fixing agents and one or more staining agents. *See id.* The staining agents may include one or more pap smear stains. *See* page 22, the paragraph beginning at line 27.

The kit may also include a surface including an array of electrodes adapted to subject particles of a sample to a dielectrophoretic force to segregate the particles into two or more zones. *See id.* In one respect, the dielectrophoretic force may arise from simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes. *See* page 8, the paragraph beginning at line 6; *see also* page 32, the paragraph beginning at line 10.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following issues are presented for review:

(1) whether claims 1-6, 13, 44, 45, and 49-50 are obvious under 35 U.S.C. § 103(a) in view of Becker (WO 01/14870) ("'870 Becker");

(2) whether claims 7-11 are obvious over the '870 Becker reference in view of Seul *et al.* (U.S. Patent No.: 6,387,707)("Seul");

(3) whether claim 12 is obvious over the '870 Becker reference in view of Giddings *et al.* (U.S. Patent No.: 4,250,026)("Giddings");

(4) whether claim 14 is obvious over the '870 Becker reference in view of Arnolds *et al.* (U.S. Patent No.: 6,673,225)("Arnold");

(5) whether claim 15 is obvious over the '870 Becker reference in view of Cheng *et al.* (U.S. Publication No.: 20020076825)("Cheng");

(6) whether claims 16-18, 20-25, 28-34, 42, and 52-54 are obvious over the '870 Becker reference in view the website of Tripath Imaging, Inc. dated March 5, 2002 ("Tripath Imaging");

(7) whether claim 19 is obvious over the '870 Becker reference and Tripath Imaging's website in view of Coster *et al.* (U.S. Patent No.: 5,589,047)("Coster");

(8) whether claims 26 and 27 are obvious over the '870 Becker reference and Tripath Imaging's website in view of Becker *et al.* (U.S. Patent No.: 5,858,192)("'192 Becker");

(9) whether claim 35 is obvious over the '870 Becker reference and Tripath Imaging's website in view Cheng;

(10) whether claims 36-40 are obvious over the '870 Becker reference and Tripath Imaging's website in view of Seul;

(11) whether claim 41 is obvious over the '870 Becker reference, Tripath Imaging's website, and Seul in view of Giddings;

(12) whether claim 43 is obvious over the '870 Becker reference and Tripath Imaging's website in view of Arnold;

(13) whether claims 46 and 47 are obvious over the '870 Becker reference in view of Seul;

(14) whether claim 48 is obvious over the '870 Becker reference in view of Giddings;

(15) whether claims 55 and 56 are obvious over the '870 Becker reference and Tripath Imaging's website; and

(16) whether claim 29 is an improper dependent claim.

VII. ARGUMENT

A. Substantial Evidence is Required to Uphold the Examiner's Position

As an initial matter, Appellant notes that findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706(A), (E), 1994. *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999). Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312.

Accordingly, an Examiner's position on Appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

B. Claims Are Patentable under 35 U.S.C. §103

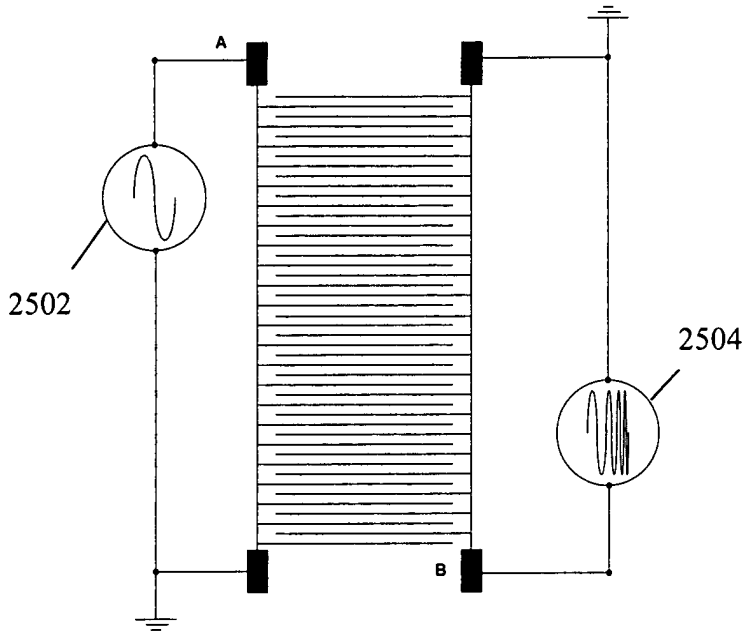
The pending claims stand rejected under 35 U.S.C. § 103(a). Appellant respectfully traverses.

1. The '870 Becker Reference Does not Render the Claims Obvious

a) Claim 1 is Not Taught or Suggested by the '870 Becker Reference

Independent claim 1 recites, in part, "subjecting particles of a sample to a dielectrophoretic force by *simultaneously applying a swept frequency signal to a first set of*

electrodes and a fixed frequency signal to a second set of electrodes." (Emphasis added). FIG. 25B illustrates a representative, but non-limiting embodiment as follows:



where

> element 2502 can correspond, in one embodiment to a 20 kHz signal generator suitable for forming a fixed frequency. Element 2504 can correspond to a 20kHz - 2 MHz FM signal generator or other generator for forming a swept frequency. (Specification, page 32, lines 14-17).

The '870 Becker reference is directed to discriminating matter using dielectrophoresis and field flow fractionation. In one respect, the '870 Becker reference discloses applying a signal with a signal frequency that changes in a step-wise fashion to separate a mixture comprising multiple subpopulations (S_1, S_2, and S_3). *See* page 44, lines 23-25. First, signals with a first frequency (f_1) "would be applied to elute subpopulation S_1, whilst ensuring slow movement of subpopulations S_2 and S_3. After subpopulation S_1 is eluted from the chamber or is moved far ahead of the other two subpopulations, subpopulation S_2 may be eluted by changing the frequency to f_2 whilst still ensuring slow movement of subpopulation S_3... [F]inally, a signal

of frequency f_3 may be applied to rapidly elute subpopulation S_3." (Page 44, line 27 through page 45, line 1). While the frequencies (f_1, f_2, or f_3) may include different frequency modulation, the frequencies applied to the mixture in the '870 Becker reference are applied in a serial, sequential fashion. *See* page 39, line 20; *see also* page 13, lines 15-16.

For example, the '870 Becker reference discloses that a sweeping frequency "may first be applied to electrodes...after such a frequency sweep step, signals of a fixed frequency may be applied to elute all the particle types remaining in the separation chamber." *See* page 44, lines 14-22. In contrast to the invention, the '870 Becker reference fails to disclose or suggest subjecting particles of a sample to a dielectrophoretic force by simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes, as recited by claim 1.

The Office's present arguments state that it would be obvious to modify the '870 Becker reference to teach the elements of claim 1. *See* page 4 of the Final Office Action. In particular, the Office cites page 49, lines17-21 of the '870 Becker reference which states: "Different electrical signals (frequency, magnitude and waveforms) are applied to the facing electrodes from the signal generator so that the particles experience different DEP forces from the field produced by each array 5," as teaching the elements of claim 1. Appellant respectfully traverses. This citation glaringly fails to teach or suggest simultaneously applying the different electrical signals to a first set of electrodes and a second set of electrodes as recited in independent claim 1.

Appellant notes that an unsubstantiated assertion does not establish a *prima facie* case of obviousness. In deriving the above inference, the Office is evidently proceeding with an impermissible hindsight analysis of the invention. This is improper under the law. To imbue one of ordinary skill in the art with knowledge of the instant invention, where no prior art

reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher. *W.L. Gore Assoc., Inc. v. Garlock, Inc.*, 220 USPQ 303, 312-313 (Fed. Cir. 1983).

In sum, the '870 Becker reference fails to teach or even suggest the elements required by pending claim 1—particularly, simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes. Notably, the Office has not been able to point to a passage in the '870 Becker reference that would teach or suggest such elements required by claim 1, and the Board is invited to look at the record for confirmation. Additionally, the Office states on page 14 of the Final Office Action, "Becker et al do not explicitly disclose the simultaneous application of a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes." Thus, claim 1 is believed to be in condition for allowance, and Appellant respectfully requests that the rejection be withdrawn.

b) Claims 2-6 and 13 are Not Taught or Suggested by the '870 Becker Reference

Claims 2-6 and 13 are rejected in view of the '870 Becker reference. Appellant submits each of these claims is patentable for independent reasons because the '870 Becker reference fails to teach or suggest the elements of these claims.

For instance, claim 2 requires (in addition to claim 1):

- the swept frequency signal falls from a maximum intensity to a minimum intensity along a length of a surface in a first direction, and the fixed frequency signal falls from a maximum intensity to a minimum intensity along the length of the surface in a second direction opposing the first direction

The Office has not provided evidence to show that the claim is not patentable; accordingly, no *prima facie* case has been established. *See* page 3 of the Final Office Action. The Office also states "Becker et al also do not explicitly disclose methods comprising the swept frequency signal falling from maximum intensity along a length of a surface, and the fixed frequency signal falling from maximum to minimum intensity in the opposite direction; linear or non-linear intensity variation; intensity controlled by the electrode bus width, or non-zero minimum intensities of either signal." (Page 14 of the Final Office Action). Appellant submits that '870 Becker reference does not teach or suggest this element, and that claim 2 is patentably distinct.

Claim 3 requires (in addition to claim 2):

- the intensities vary linearly along the length of the surface

The Office cites page 11, lines 10-17 of the '870 Becker reference. However, this passage is directed to the ratio of electrode height and width and in altering this ratio, the levitation of a matter is changed. As such, a *prima facie* case has not been established.

Additionally, the Office states that the '870 Becker reference does not disclose the linear intensity variation. *See* page 14 of the Final Office Action. Appellant submits that claim 3 is patentably distinct over the '870 Becker reference.

Claim 4 requires (in addition to claim 2):

- the intensities vary non-linearly along the length of the surface

Similar to claim 3, the Office relies on the passage relating to the ratio of an electrode. However, the Office contradicts this argument and states that the '870 Becker reference does not disclose the non-linear intensity variation. *See id.* Appellant submits that the '870 Becker reference does not teach or suggest this element.

Claim 5 requires (in addition to claim 2):

- the intensities are varied by varying a width of electrode buses with distance along a length of the surface

The '870 Becker reference does not teach or suggest that the intensities of signals are varied with distance along the length of the surface as recited in claim 5. The Office has not pointed out passages that teach or suggest this element. As such, a *prima facie* case has not been established.

Additionally, the Office states that the '870 Becker reference does not disclose the intensities are controlled by the electrode bus width. *See id.* Appellant submits that the '870 Becker reference does not teach or suggest this element.

Claim 6 requires (in addition to claim 2):

- the minimum intensity of the swept frequency or fixed frequency signal is non-zero

The Office has not established a *prima facie* case, as the Office has failed to provide passages within the '870 Becker reference that teaches or suggest this element.

Additionally, the Office recognizes that the '870 Becker reference does not disclose the minimum of either intensities. *See id.*

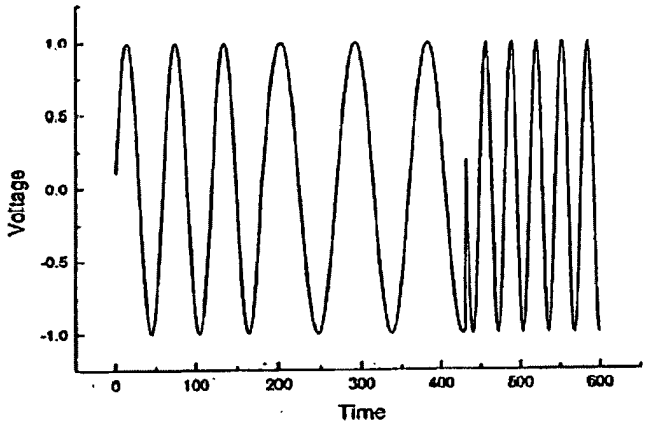
These additional and important distinctions between the '870 Becker references and the invention further exemplifies that the present claims are patentable, despite the current rejections.

c) Claim 44 is Not Taught or Suggested by the '870 Becker Reference

Independent claim 44 recites, in part, "*a first signal generator configured to apply a fixed frequency signal to a first electrode... a second signal generator configured to apply a swept frequency signal to a second electrode...* where the fixed frequency signal and the swept frequency signal are applied *simultaneously*" (emphasis added). Such features are nowhere taught or suggested in the '870 Becker reference.

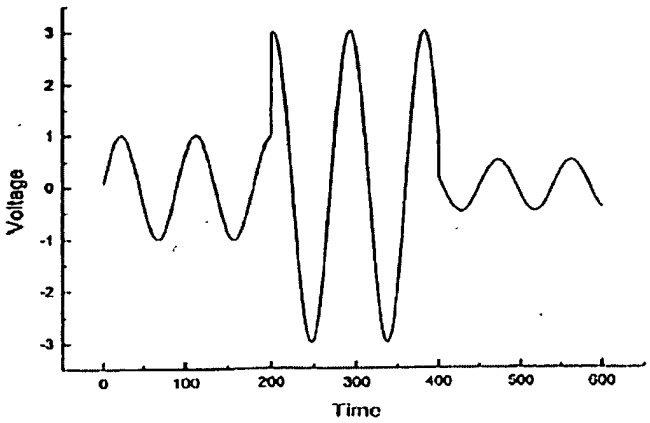
The Office relies upon page 45, lines 3-8 and again to page 49, lines 17-21 of the '870 Becker reference and alleges that these passages teach or suggest the elements of claim 44. *See* page 6 of the Final Office Action. Appellant respectfully traverses.

The '870 Becker reference discloses on page 45, lines 3-8 that signals having two or more components (*e.g.,* having frequencies f1 and f2 or intensities V1 and V2) may be applied simultaneously, as shown, *e.g.,* in FIGS. 6B and 6C shown below.



Fixed Amplituide,
Three Frequencies: f1,f2,f3

FIG. 6B



Fixed Frequency,
Three Amplitudes: V1,V2,V:

FIG. 6C

The application of the above signals are not the same as a fixed frequency signal and a swept signal being applied simultaneously, as recited in claim 44.

Additionally, the '870 Becker reference does not teach or suggest, or provide motivation for simultaneously applying a signal to a first electrode and another to a second electrode. The citation on page 49, lines 10-21 merely suggests applying *one* signal from the *one* signal generator and modifying that one signal (*e.g.,* changing the frequency, magnitude, or waveform). There is no teaching or suggestion concerning a first signal generator configured to apply a fixed frequency signal to a first electrode... a second signal generator configured to apply a swept frequency signal to a second electrode... where the fixed frequency signal and the swept frequency signal are applied simultaneously, as recited in claim 44.

Thus, in view of at least these independent reasons, there can be no *prima facie* case of obviousness; claim 44 is in condition for allowance, and the rejection should be withdrawn.

d) Claim 49 is Not Taught or Suggested by the '870 Becker Reference

Independent claim 49 recites, in part: a dielectrophoretic field flow fractionator configured to subject particles of a sample to a dielectrophoretic force by *simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes.* (Emphasis added). Similar to the rejections made to independent claims 1 and 44, the Office relies on the page 49, lines 10-21 as support for the "simultaneous application of two different signals to tow set of electrodes." *See* page 7. As noted above, the cited passage does not teach or suggest simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes.

Thus, in view of at least these independent reasons, there can be no *prima facie* case of obviousness; claim 49 is in condition for allowance, and Appellant respectfully requests that the rejection should be withdrawn.

2. The Secondary References Do Not Render the Claims Obvious

a) The Seul Reference Does Not Provide the Deficiencies of the '870 Becker Reference

Claims 7-11 stand rejected under 35 U.S.C. § 103 in view of the '870 Becker and Seul references. Appellant respectfully traverses.

Claims 7-11, which are dependent from claim 1, are patentably distinct over the '870 Becker reference for at least the same reasons outlined above. Additionally, while the Seul reference contemplates spatial manipulation of colloidal particles and molecules, the Seul reference does not augment the deficiencies of '870 Becker reference.

The Seul reference discloses three elements used for manipulation: 1) an AC electric field-induced assembly; 2) spatial modulation of the interfacial impedance; and 3) real-time, interactive control over the state of the interfacial impedance by light. *See* Summary of Invention. The first element allows particles or molecules to respond to one AC electric signal. For example, FIG 2b illustrates an electric field (10Vp-p, 1kHz) that captures beads in the thin oxide region 22. *See* FIG. 2A; *see also* Example X, "Alignment and Stretching of DNA in Electric Field-Induced Flow"; *see also* FIGS. 12 through 15 and supporting text. Seul does not propose or suggest applying a particular, second signal. Seul does not need, desire, or require subjecting particles of a sample to a dielectrophoretic force by simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes because the three elements, including applying one AC field, are treated as being sufficient for parsing particles and molecules. Therefore, Becker and Seul, either separately or combined, do not teach or suggest all the elements of claim 1.

As noted in the Final Office Action, the Office agrees that the secondary references (including the Seul reference) fail to provide the deficiencies of the '870 Becker reference. *See*

page 26 of the Final Office Action. For at least the above reasons, claims 7-11 are in condition for allowance, and the rejection should be withdrawn.

b) The Seul Reference Does Not Teach or Suggest Claims 7-11, Claims 36-41, Claim 46, and Claim 47

As noted by the Office, the '870 Becker reference does not teach the elements of claims 7-11. *See* page 9 of the Final Office Action. Claims 36-40 recite similar limitations to claims 7-11, respectively. Claim 46 recites a limitation similar to claim 10 and claim 47 recites a limitation similar to claim 11. Applicants submit that the Seul reference fails to teach or suggest these elements.

For example, claim 7 requires (in addition to claim 1):

- filtering the sample by subjecting particles of the sample to a flow, a cross flow, and a dielectrophoretic force that opposes a force associated with the cross flow

The Office relies on FIG. 9A and column 19, line 45 through column 20, line 15 as allegedly teaching or suggesting claim 7. *See id.* However, this passage fails to teach or suggest filtering the sample by subjection the *a flow, a cross flow, and a dielectrophoretic force* that opposes a force associated with the cross flow. As such, a *prima facie* case has not been established.

Appellant submits that claims 7-11, 36-40, 46, and 47 are each patentable over the Seul and/or '870 Becker references.

c) The Giddings Reference Does Not Provide the Deficiencies of the '870 Becker Reference

Claim 12 stands rejected under 35 U.S.C. § 103 in view of the '870 Becker and Giddings references. Appellant respectfully traverses.

Referring to FIG. ONE of Giddings, a sedimentation force, represented by vector F, is applied in one direction. Giddings discloses that "the device is tilted by use of rotational means 14 about an axis of rotation 16 so that the particles will sediment slowly across the enlarged

width..." (Column 4, lines 4-6). Giddings notes that with the device on a tilt, the particles are "subject only to sedimentation forces [and] would distribute themselves over the thickness of the channel and would therefore be subjected to flow displacement velocities ranging from near zero at the wall to the maximum flow velocity at the center of the channel." (Column 4, lines 19-24). Nowhere in the disclosure of Giddings is a dielectrophoretic force mentioned and, more pertinently, Giddings does not cure the lack of disclosure or suggestion concerning subjecting particles of a sample to a dielectrophoretic force by simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes in the '870 Becker reference.

As noted in the Final Office Action, the Office agrees that the secondary references (including the Giddings reference) fail to provide the deficiencies of the '870 Becker reference. *See* page 26 of the Final Office Action. For at least the above reasons, claim 12 is in condition for allowance, and the rejection should be withdrawn.

d) The Giddings Reference Does Not Teach or Suggest Claims 12, 41, and 48

Claim 12 requires (in addition to claim 1)

- where attaching the particles into two or more zones comprises confining particles in a particular zone using a physical barrier.

Claims 41 and 48 recite a similar limitation. The Office notes that the '870 Becker reference fails to disclose the elements of claim 12. *See* page 10 of the Final Office Action. The Office contends that the Abstract and FIG. 1 of the Giddings reference teaches or suggests this element. However, the citation does not provide disclosure regarding *attaching* the particles into two or more zones comprises confining particles in a particular zone using a physical barrier. Thus, the Giddings reference, separately or in combination with the '870 Becker reference, fails to teach or

suggest the elements of claim 12. Appellant submits that claims 12, 41, and 48 are patentable over the Giddings and/or '870 Becker references.

e) The Arnold Reference Does Not Provide the Deficiencies of the '870 Becker Reference

Claim 14 stands rejected under 35 U.S.C. § 103(a) in view of the '870 Becker and Arnold references. Appellant respectfully traverses.

Arnold involves applying negative dielectrophoretic forces to separate, collect, and/or manipulate particles or cells. *See* Abstract. However, the disclosure of Arnold, either separately or in combination with the '870 Becker reference, does not teach or suggest subjecting particles of a sample to a dielectrophoretic force by simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes. Arnold discloses different electrode configurations that can be used to apply an electric field to a sample. However, only one signal is applied where the "voltage applied to the electrodes to create the electric field within the medium is preferably an alternating voltage of a frequency in the range 100 Hz to 1000 MHz and more preferably in the range 10 kHz to 300 MHz, and may generate a field strength within the medium in the range 10 V/mm to 100 V/mm." (Column 3, line 67 through Column 4, line 3).

As noted in the Final Office Action, the Office agrees that the secondary references (including the Arnold reference) fail to provide the deficiencies of the '870 Becker reference. *See* page 26 of the Final Office Action. For at least the above reasons, claim 14 is in condition for allowance, and the rejection should be withdrawn.

f) The Cheng Reference Does Not Provide the Deficiencies of the '870 Becker Reference

Claim 15 stands rejected under 35 U.S.C. § 103(a) in view of the '870 Becker and Cheng references. Appellant respectfully traverses.

The Cheng reference discloses focusing moieties using dielectrophoresis, specifically traveling-wave dielectrophoresis. *See* page 21, paragraph 230. Separate groups of electrodes receive a separate AC signal with the same frequency but with a different phase. A dielectrophoretic force is not provided by simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes, as recited by claim 1.

As noted in the Final Office Action, the Office agrees that the secondary references (including the Cheng reference) fail to provide the deficiencies of the '870 Becker reference. *See* page 26 of the Final Office Action. For at least the above reasons, claim 15 is in condition for allowance, and the rejection should be withdrawn.

g) The Cheng Reference Does Not Teach or Suggest Claims 15 and 35

Claim 15 requires (in addition to claim 1):

- automatically adjusting the swept frequency signal or fixed frequency signal as a function of conductivity of a particle suspending medium.

Claim 35 recites a similar limitation. The Office relies on the Cheng reference, and in particular, paragraphs 0004 and 0057-0059. *See id.* These passages, while contemplating an automated integrated system, fails to provide disclosure relating to automatically adjusting the swept frequency signal or fixed frequency signal as a function of conductivity of a particle suspending medium. Thus, the Cheng reference, separately or in combination with the '870 Becker reference, fails to teach or suggest the elements of claim 15. Appellant submits that claims 15 and 35 are patentable over the Cheng and/or '870 Becker references.

h) The Tripath Imaging Website Does Not Provide the Deficiencies of the '870 Becker Reference

Claims 16-18, 20-25, 28-34, 43, 52, and 54 stand rejected under 35 U.S.C. § 103(a) in view of the '870 Becker reference and the Tripath Imaging's website. Appellant respectfully traverses.

Independent claim 16, recites:

> A method comprising:
> subjecting particles of a sample to a dielectrophoretic force to segregate the particles into two or more zones of a surface by simultaneously applying a swept frequency signal applied to a first set of electrodes and a fixed frequency signal to a second set of electrodes;
> attaching the particles to the surface, thereby defining a segregated smear; and
> fixing or staining the segregated smear.

Claim 16 recites a similar limitation as independent claim 1. As noted above, the '870 Becker reference does not teach or suggest such a limitation. The Tripath Imaging's website does not supply features absent from Becker. The PrepStain ™ uses a process that combines gravity dispersion and centrifugation to separate debris from a diagnostic material. The website and Becker, either separately or in combination, do not teach all the elements of independent claim 16.

Since independent claim 49 recites a similar limitation to claim 16 and the '870 Becker reference and/or the Tripath Imaging website fail to teach or suggest such elements. Appellant respectfully asserts that claim 49 is allowable.

As noted in the Final Office Action, the Office agrees that the secondary references (including the Tripath Imaging website) fail to provide the deficiencies of the '870 Becker reference. *See* page 26 of the Final Office Action. For at least the above reasons, claim 16 and 49, and their respective dependent claims, are in condition for allowance, and the rejections should be withdrawn.

i) The Coster Reference Does Not Provide the Deficiencies of the '870 Becker Reference

Claim 19 stands rejected under 35 U.S.C. § 103(a) in view of the '870 Becker reference, Tripath Imaging's website, and the Coster reference. Appellant respectfully traverses.

The Coster reference describes methods for separating, selecting, and/or, fusing cells. Coster discloses applying a dielectrophoretic force on the cells as "the frequency of an alternating electric field is applied to the cell 10." Column 8, lines 10-12. Coster apparently applies only one signal with one frequency to the cells.

As noted in the Final Office Action, the Office agrees that the secondary references (including the Coster reference) fail to provide the deficiencies of the '870 Becker reference. *See* page 26 of the Final Office Action. For at least the above reasons, claim 19 is in condition for allowance as independent claim 1, and the rejections should be withdrawn.

j) The Coster Reference Does Not Teach or Suggest Claim 19

Claim 19 requires (in addition to claim 16)

- attaching comprising using an adhesive coupled to the surface.

The Office notes that neither the Tripath Imaging's website or the '870 Becker reference teach or suggest the elements of claim 19. *See* page 17 of the Final Office Action. The Office provides an unsubstantiated argument that the Coster reference provides this element without noting specific passages or figures. *See id.* Appellant submits that the mere recitation that a reference teaches or suggests an element does not satisfy a *prima facie* case of obviousness.

Appellant believes claim 19 is independently patentable over the cited references and respectfully requests the removal of the rejection.

k) The '192 Becker Reference Does Not Provide the Deficiencies of the '870 Becker Reference

Claims 26 and 27 stand rejected under 35 U.S.C. § 103(a) in view of the '870 Becker reference, the Tripath Imaging's website, and the '192 Becker reference. Appellant respectfully traverses.

The '192 Becker reference teaches manipulating matter using an electric field (from a cDEP force and a twDEP force) and/or externally applied fluid flow forces. Referring to FIG. 2A and 2B of the '192 reference, an "electric field can be applied to the electrode elements 5 creates conventional dielectrophoretic forces on the particles in accordance with their dielectric and conductive properties as well as those of the carrier medium." Column 18, lines 42 through 46. Chamber 10 of FIG. 2A and 2B also utilizes twDEP forces in addition to cDEP forces, thereby displacing matter in two-dimensions (vertical and horizontal). *See* column 19, lines 30-32. A dielectrophoretic force is not provided by simultaneously applying a swept frequency signal applied to a first set of electrodes and a fixed frequency signal to a second set of electrodes.

As noted in the Final Office Action, the Office agrees that the secondary references (including the '192 Becker reference) fail to provide the deficiencies of the '870 Becker reference. *See* page 26 of the Final Office Action. For at least the above reasons, claims 26 and 27 are in condition for allowance, and the rejections should be withdrawn.

l) Claims 35-41, 43, 46-48, 55, and 56

Claims 35-41, 43, 46-48, 55, and 56 stand rejected under 35 U.S.C. § 103(a) in view of the '870 Becker reference and a combination of the secondary references. As outlined above, neither the '870 Becker reference and/or any of the secondary references, separately or in combination, teach or suggest the elements of the independent claims. For example, the cited

references lack disclosure teaching or suggesting simultaneously applying a fixed frequency signal to a first electrode and a second frequency signal to a second electrode (or similar limitations) as specifically recited in independent claims 16, 44, 49, and 50.

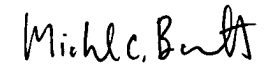
For at least the above reasons, claims 16, 44, 49, and 50, and their respective dependent claims are in condition for allowance, and the rejections should be withdrawn.

CONCLUSION

Appellant has provided arguments that overcome all the pending rejections. Appellant respectfully submits that the Final Office Action's conclusions that the claims should be rejected are unwarranted. It is therefore requested that the Board overturn the rejections.

Please date stamp and return the enclosed postcard to evidence receipt of this document.

Respectfully submitted,



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Date: January 31, 2006

CLAIMS APPENDIX

1. (Previously Amended) A method comprising:

subjecting particles of a sample to a dielectrophoretic force by simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes;

segregating the particles into two or more zones of a surface; and

attaching the particles to the surface.

2. (Original) The method of claim 1, where the swept frequency signal falls from a maximum intensity to a minimum intensity along a length of a surface in a first direction, and the fixed frequency signal falls from a maximum intensity to a minimum intensity along the length of the surface in a second direction opposing the first direction.

3. (Original) The method of claim 2, where the intensities vary linearly along the length of the surface.

4. (Original) The method of claim 2, where the intensities vary non-linearly along the length of the surface.

5. (Original) The method of claim 2, where the intensities are varied by varying a width of electrode buses with distance along a length of the surface.

6. (Original) The method of claim 2, where the minimum intensity of the swept frequency or fixed frequency signal is non-zero.

7. (Original) The method of claim 1, further comprising filtering the sample by subjecting particles of the sample to a flow, a cross flow, and a dielectrophoretic force that opposes a force associated with the cross flow.

8. (Original) The method of claim 7, where the flow and cross flow are substantially perpendicular to one another.

9. (Original) The method of claim 7, where the flow and cross flow are not perpendicular.

10. (Original) The method of claim 7, where the dielectrophoretic force arises from the excitation of electrodes near a dielectric substrate having openings.

11. (Original) The method of claim 7, where the dielectrophoretic force arises from current passing through an opening in a dielectric barrier.

12. (Previously Amended) The method of claim 1, where attaching the particles into two or more zones comprises confining particles in a particular zone using a physical barrier.

13. (Original) The method of claim 1, where segregating the particles comprises flow DEP-FFF.

14. (Original) The method of claim 1, further comprising promoting growth of particles on the surface.

15. (Original) The method of claim 1, further comprising automatically adjusting the swept frequency signal or fixed frequency signal as a function of conductivity of a particle suspending medium.

16. (Previously Amended) A method comprising:

subjecting particles of a sample to a dielectrophoretic force to segregate the particles into two or more zones of a surface by simultaneously applying a swept frequency signal applied to a first set of electrodes and a fixed frequency signal to a second set of electrodes;

attaching the particles to the surface, thereby defining a segregated smear; and

fixing or staining the segregated smear.

17. (Original) The method of claim 16, comprising fixing and staining the segregated smear.

18. (Original) The method of claim 16, the attaching comprising subjecting the particles to a dielectrophoretic force.

19. (Original) The method of claim 16, the attaching comprising using an adhesive coupled to the surface.

20. (Original) The method of claim 16, the attaching comprising allowing the particle to settle on the surface.

21. (Original) The method of claim 16, the particles comprising cells.

22. (Original) The method of claim 16, the smear comprising a pap smear.

23. (Original) The method of claim 16, where subjecting particles to a dielectrophoretic force comprises subjecting the particles to a dielectrophoretic force arising from the simultaneous application of programmed voltage signals of different frequencies.

24. (Original) The method of claim 16, where subjecting particles to a dielectrophoretic force comprises subjecting the particles to a dielectrophoretic force arising from the application of frequencies exhibiting one or more DEP-FFF and trapping phases.

25. (Original) The method of claim 16, where subjecting particles to a dielectrophoretic force comprises subjecting the particles to dielectrophoretic forces generated by electrodes coupled to the surface.

26. (Original) The method of claim 25, the electrodes comprising spiral electrodes.

27. (Original) The method of claim 16, the two or more zones comprising concentric circular zones.

28. (Original) The method of claim 16, the two or more zones comprising distinct bands of particles.

29. (Original) The method of claim 16, where subjecting particles of the sample to a dielectrophoretic force comprises using a swept frequency signal in combination with a fixed frequency signal.

30. (Original) The method of claim 29, where the swept frequency signal falls from a maximum intensity to a minimum intensity along a length of a surface in a first direction, and the fixed frequency signal falls from a maximum intensity to a minimum intensity along the length of the surface in a second direction opposing the first direction.

31. (Original) The method of claim 30, where the intensities vary linearly along the length of the surface.

32. (Original) The method of claim 30, where the intensities vary non-linearly along the length of the surface.

33. (Original) The method of claim 30, where the intensities are varied by varying a width of electrode buses with distance along a length of the surface.

34. (Original) The method of claim 30, where the minimum intensities of the swept frequency and fixed frequency signals are non-zero.

35. (Original) The method of claim 29, further comprising automatically adjusting the swept frequency signal or fixed frequency signal as a function of conductivity of a particle suspending medium.

36. (Original) The method of claim 16, further comprising filtering the sample by subjecting particles of the sample to a flow, a cross flow, and a dielectrophoretic force that opposes a force associated with the cross flow.

37. (Original) The method of claim 36, where the flow and cross flow are substantially perpendicular to one another.

38. (Original) The method of claim 36, where the flow and cross flow are not perpendicular.

39. (Original) The method of claim 36, where the dielectrophoretic force arises from the excitation of electrodes near a dielectric substrate having openings.

40. (Original) The method of claim 36, where the dielectrophoretic force arises from current passing through an opening in a dielectric barrier.

41. (Original) The method of claim 36, where attaching the particles into two or more zones comprises use of a physical barrier to confine particles in a particular zone.

42. (Original) The method of claim 16, where particles are segregated using flow DEP-FFF.

43. (Original) The method of claim 16, further comprising promoting growth of particles on the surface.

44. (Previously Amended) An apparatus comprising:

a surface;

electrodes near the surface;

a first signal generator configured to apply a fixed frequency signal to a first electrode, the fixed frequency signal falling from a maximum intensity to a minimum intensity along a length of the surface in a first direction;

a second signal generator configured to apply a swept frequency signal to a second electrode, the swept frequency signal falling from a maximum intensity to a minimum intensity along the length of the surface in a second direction opposing the first direction, where the fixed frequency signal and the swept frequency signal are applied simultaneously; and

where applying the swept frequency signal in combination with the fixed frequency signal generates a dielectrophoretic force configured to segregate particles into two or more zones of the surface.

45. (Original) The apparatus of claim 44, where the first and second signal generators are integral.

46. (Original) The apparatus of claim 44, further comprising a filter coupled to the surface, the filter configured to subject particles of a sample to a flow, a cross flow, and a dielectrophoretic force that opposes a force associated with the cross flow.

47. (Original) The apparatus of claim 46, the filter comprising electrodes near a dielectric substrate having openings.

48. (Original) The apparatus of claim 44, further comprising a physical barrier near the surface configured to attach particles into two or more zones of the surface.

49. (Previously Amended) An apparatus for preparing a smear for cytopathology, comprising:

a dielectrophoretic field flow fractionator configured to subject particles of a sample to a dielectrophoretic force by simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes to segregate the particles into two or more zones; and

a dielectrophoretic collector coupled to the fractionator configured to subject the particles to a dielectrophoretic force to attach the particles to a surface.

50. (Original) The apparatus of claim 49, the smear comprising a pap smear.

51. (Original) The apparatus of claim 49, where the fractionator and collector form an integral unit.

52. (Original) The apparatus of claim 49, further comprising a machine reader coupled to the fractionator or collector and configured to evaluate particles within the two or more zones.

53. (Original) The apparatus of claim 49, further comprising a fixing stage and a staining stage coupled to the collector.

54. (Original) The apparatus of claim 53, where the fixing and staining stages are coupled to the collector to form an integral unit.

55. (Previously Amended) A kit in a suitable container for preparing a smear for cytopathology, comprising:

a surface comprising an array of electrodes adapted to subject particles of a sample to a dielectrophoretic force by simultaneously applying a swept frequency signal to a first set of electrodes and a fixed frequency signal to a second set of electrodes to segregate the particles into two or more zones;

one or more fixing agents; and

one or more staining agents.

56. (Original) The kit of claim 55, the one or more staining agents comprising one or more pap smear stains.

EVIDENCE APPENDIX

None

RELATED PROCEEDINGS APPENDIX

None